Office Action Summary

Application No.	Applicant(s)
09/485,298	Yamamoto et al.
Examiner	**Art Unit**
Arun Chakrabarti	1655

-- **The MAILING DATE of this communication appears on the cover sheet with the correspondence address** --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Feb 15, 2002 .

2a) ☐ This action is **FINAL.** 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 20-39 is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 20-39 is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

15) ☒ Notice of References Cited (PTO-892)

16) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

17) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

18) ☐ Interview Summary (PTO-413) Paper No(s). _____

19) ☐ Notice of Informal Patent Application (PTO-152)

20) ☐ Other:

DETAILED ACTION

Specification

1. In view of the argument of the applicant in the interview summary of paper number 17, the finality of the previous office action is hereby withdrawn. It is however noted that Hong et al. (U.S. Patent 6,165, 765) (December 26, 2000) gets it priority back to application number 08/544,643.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

3. Claims 31, 32, 34, and 35 are rejected under 35 U.S.C. 102 (e) as being anticipated by Huse et al. (U.S. Patent 5,681,726) (October 28, 1997).

Huse et al teach at least one nucleotide analog to be incorporated in place of dGTP, dCTP, dATP, and dTTP and a reagent for synthesizing in the presence of nucleotide analog a cDNA that is complementary to an RNA (Claim 8, Figure 1, and Column 12, lines 25-31).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 20-25, 27-29, 31, 32, 34, 35 and 38-39 are rejected under 35 U.S.C 103 (a) over Huse et al. (U.S. Patent 5,681,726) (October 28, 1997) in view of Hong et al. (U.S. Patent 5,747,298) (May 5, 1998).

Huse et al teach a method and kit for amplifying a DNA by polymerase chain reaction by the use of a DNA fragment comprising a nucleotide analog as a template (Claim 8, Figure 1, and Column 12, lines 25-31).

Huse et al teach a method for amplifying a DNA characterized in that the DNA fragment is a cDNA prepared by reverse transcription reaction using an RNA as a template (Claim 8, Figure 1, and Column 12, lines 25-31)

Huse et al do not teach the method for amplifying a DNA in the presence of two or more kinds of nucleotide analogs, wherein the nucleotide analogs are uniformly incorporated into the resulting DNA, thereby selectively amplifying DNA of a target sequence.

Hong et al teach the method for amplifying a DNA in the presence of two or more kinds of nucleotide analogs, wherein the nucleotide analogs are uniformly incorporated into the resulting DNA, thereby selectively amplifying DNA of a target sequence (Column 3, lines 4-23).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the method for amplifying a DNA in the presence of two or more kinds of nucleotide analogs, wherein the nucleotide analogs are uniformly incorporated into the resulting DNA, thereby selectively amplifying DNA of a target sequence of Hong et al with the methods of amplifying nucleic acids using modified nucleotide template of Dower et al ., since Hong et al state, "In the past few years since this enzyme was made commercially available under the name of Bst DNA polymerase, independent reports have confirmed that during sequencing reaction catalyzed by this enzyme all four dNTPs, including dCTP, and other nucleotide analogs, such as dITP and 7-deazadGTP, are incorporated equally effectively in the chain elongation, thus eliminating the weak "C" band phenomena often observed when other DNA polymerases are used, and producing a very good band uniformity on

the sequencing gel (Column 3, lines 4-13)". An ordinary artisan would have been motivated by these express statements of Hong et al to substitute and combine the method for amplifying a DNA in the presence of two or more kinds of nucleotide analogs, wherein the nucleotide analogs are uniformly incorporated into the resulting DNA, thereby selectively amplifying DNA of a target sequence of Hong et al with the methods of amplifying nucleic acids using modified nucleotide template of Dower et al ., in order to achieve the express advantages of modified nucleotide analogues, as noted by Hong et al , which provides a method that confirmed that during sequencing reaction catalyzed by a particular polymerase enzyme all four dNTPs, including dCTP, and other nucleotide analogs, such as dITP and 7-deazadGTP, are incorporated equally effectively in the chain elongation, thus eliminating the weak "C" band phenomena often observed when other DNA polymerases are used, and producing a very good band uniformity on the sequencing gel.

6. Claims 20-30, 31, 32, 34, 35 and 38-39 are rejected under 35 U.S.C 103 (a) over Huse et al. (U.S. Patent 5,681,726) (October 28, 1997) in view of Hong et al. (U.S. Patent 5,747,298) (May 5, 1998). further in view of Dodge et al. (U.S. Patent 5,912,117) (June 15, 1999).

Huse et al in view of Hong et al teach the method of claims 20-25, 27-29, 31, 32, 34, 35 and 38-39 as described above.

Dower et al in view of Hong et al do not teach the compounds for lowering the *Tm* value of a double-stranded nucleic acid.

Dodge et al teach the compounds (glycerol and DMSO) for lowering the *Tm* value of a double-stranded nucleic acid.(Column 8, line 49 to column 9, line 4).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to substitute and combine the compounds for lowering Tm of duplex DNA of Dodge et al with the fast and accurate methods of amplifying nucleic acids using modified nucleotide template and nucleotides of Dower et al in view of Honget al., since Dodge et al state, "To assure PCR efficiency, glycerol and other related solvents such as dimethyl sulfoxide, can be used to increase the sensitivity of the PCR at the amplification level and to overcome problems pertaining to the sequencing of regions of DNA having strong secondary structure. These problems may include : (1) low efficiency of the PCR, due to a high frequency of templates that are not fully extended by the polymerizing agent or (2) incomplete denaturation of the duplex DNA at high temperatures, due to high GC content. The use of such solvents increases the sensitivity of the assay at the level of amplification to approximately several femtograms of DNA (which is believed to correspond to a single spirochete cell). This level of sensitivity eliminates the need to detect amplified target DNA using a probe, and thereby dispenses with the requirements for radioactive probes, gel electrophoresis, Southern blotting, filter hybridization, washing and autoradiography (Column 8, line 49 to column 9, line 2)". An ordinary artisan would have been motivated by these express statements of Dodge et al to substitute and combine the compounds for lowering Tm of duplex DNA of Dodge et al with the fast and accurate methods of amplifying nucleic acids using modified nucleotide template and

nucleotides of Dower et al in view of Hong et al., in order to achieve the express advantages of solvents, as noted by Dodge et al , which provides assurance of PCR efficiency and increases the sensitivity of the PCR at the amplification level to overcome problems pertaining to the sequencing of regions of DNA having strong secondary structure including : (1) low efficiency of the PCR, due to a high frequency of templates that are not fully extended by the polymerizing agent or (2) incomplete denaturation of the duplex DNA at high temperatures, due to high GC content and in addition, increases the sensitivity of the assay at the level of amplification to approximately several femtograms of DNA (which is believed to correspond to a single spirochete cell) which eliminates the need to detect amplified target DNA using a probe, and thereby dispenses with the requirements for radioactive probes, gel electrophoresis, Southern blotting, filter hybridization, washing and autoradiography.

7. Claims 20-39 are rejected under 35 U.S.C 103 (a) over Huse et al. (U.S. Patent 5,681,726) (October 28, 1997) in view of Hong et al. (U.S. Patent 5,747,298) (May 5, 1998). further in view of Dodge et al. (U.S. Patent 5,912,117) (June 15, 1999) further in view of Stratagene Catalog (1988, Page 39).

Huse et al. in view of Hong et al. further in view of Dodge et al. expressly teach the method and kit claims of 20-32, 34, 35 and 38-39 including all the modified nucleotide templates, analogues and compounds for lowering the *Tm* value of a double-stranded nucleic acid as described above in detail.

Dower et al. in view of Hong et al. further in view of Dodge et al do not teach the motivation to combine all the reagents including DMSO and deazaATp and deazaGTP for amplifying a nucleic acid in the form of a kit.

Stratagene catalog teaches a motivation to combine reagents into kit format (page 39).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine a suitable container and all the modified nucleotide templates, analogues and compounds for lowering the *Tm* value of a double-stranded nucleic acid as taught by Dower et al. in view of Hong et al. further in view of Dodge et al, into a kit format as discussed by Stratagene catalog since the Stratagene catalog teaches a motivation for combining reagents of use in an assay into a kit, "Each kit provides two services: 1) a variety of different reagents have been assembled and pre-mixed specifically for a defined set of experiments. Thus one need not purchase gram quantities of 10 different reagents, each of which is needed in only microgram amounts, when beginning a series of experiments. When one considers all of the unused chemicals that typically accumulate in weighing rooms, desiccators, and freezers, one quickly realizes that it is actually far more expensive for a small number of users to prepare most buffer solutions from the basic reagents. Stratagene provides only the quantities you will actually need, premixed and tested. In actuality, the kit format saves money and resources for everyone by dramatically reducing waste. 2) The other service provided in a kit is quality control". (page 39, column 1).

Response to Arguments

8. Applicant's arguments with respect to claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

9. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Jones, can be reached on (703) 308-1152. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Arun Kr. Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER

Arun Chakrabarti,

Patent Examiner,

February 15, 2002